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DIHYDROMYRICETIN 3-*O*-RHAMNOSIDE FROM LEAVES OF *CATHA EDULIS*

M. GELLÉRT*, K. SZENDREI* and J. REISCH†

* Department of Pharmacognosy, University Medical School Szeged, H-6701 Szeged, Pf. 121, Hungary; † Institute of Pharmaceutical Chemistry, Westfalian Wilhelms University, D-4400, Münster/Westf. Hittorfstrasse 58–62, West Germany

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Key Word Index—*Catha edulis*; Celastraceae; dihydroflavonols; dihydromyricetin 3-*O*-rhamnoside.

Catha edulis (known locally as khat) is a shrub indigenous to large parts of East Africa. It is extensively cultivated in countries of this region and in the Arabian Peninsula, where the inhibitants chew the fresh leaves and stem tips for their stimulating effects. The chewing of khat is considered to be damaging to health and also to cause serious economic and social problems [1–3]. While the stimulating effect of khat is known to be due to the presence of phenylalkylamine-type compounds [4–6], the gastrointestinal effects (gastritis, constipation, cirrhosis of the liver) [2, 3, 7] have not been explained. Paris and Moyse-Mignon [8] reported the presence of considerable quantities of condensed tannins in the leaves and a subsequent attempt to characterize these tannins led to the detection of kaempferol, quercetin, myricetin and eight other unidentified flavonoid components [9]. The present paper deals with the isolation and characterization of dihydromyricetin (ampelopsin) and its 3-*O*-rhamnoside, a new natural product.

Dihydromyricetin (**1**) was identified on the basis of its physical constants and spectral characteristics. The glycoside (**2**) gave dihydromyricetin and rhamnose (mole ratio 1:1) on acidic hydrolysis. The position of the rhamnose was deduced from the UV and mass spectra of **2**, its aglycone and its pentamethyl ether (see Experimental). **2** was therefore identified as dihydromyricetin 3-*O*-rhamnoside. Dihydromyricetin is a rare member of the dihydroflavonol family, which has been found in relatively few plant species. The 3-*O*-rhamnoside is reported for the first time and appears to be the only known glycoside of this dihydroflavonol.

EXPERIMENTAL

Plant. Catha edulis Forsk. white variety, Celastraceae. A voucher specimen has been deposited at De Candolle Herbarium, Geneva, Switzerland.

Extraction and isolation. Fresh leaves and young twigs (4 kg) purchased from the market in Sanaa (Yemen) were extracted with MeOH (40 l.) in a blender, the extract filtered and the plant material further extracted by percolation with MeOH (15 l.). The combined extracts were concd under red. pres. to 6 l. and successively extracted with C_6H_6 (4 × 6 l.) and Et_2O (5 × 6 l.). The ppt. formed during Et_2O extraction was collected by centrifugation and eluted with MeOH. The concd MeOH soln (250 ml) gave a yellow flavonoid ppt. which was collected and washed with C_6H_6. The H_2O phase was further concd *in vacuo* to 4 l., kept in the cold for 7 days during which a ppt. formed. This flavonoid mixture was combined with the above ppt. (total wt 33.7 g). The filtrate from the H_2O phase was adjusted to pH 9 (conc. NH_4OH) and quickly extracted with $CHCl_3$ (5 × 8 l.) to remove the phenylalkylamine derivatives. The remaining H_2O phase was neutralized with HOAc and extracted with EtOAc (3 × 8 l.) and the EtOAc extracts dried (Na_2SO_4), filtered and evapd to dryness. The residue (67 g) was combined with the above ppts to give a crude flavonoid mixture, which was further purified. 30 g of the flavonoid mixture was chromatographed on a polyamide column (150 g, Woelm). Elution with H_2O afforded a yellow solid A (2.5 g) and elution with 40 % MeOH yielded 1 g of a yellow solid B.

Compound A was further purified by repeated column chromatography (Sephadex LH-20) to yield dihydromyricetin 3-rhamnoside (**2**) (0.175 g) as white needles from aq. MeOH, mp 192–195°, violet colour with $FeCl_3$, brownish red with Echtblausalz B. UV λ_{max}^{MeOH} nm: 292.5, 346; $+AlCl_3$: 313, 380; $+AlCl_3/HCl$: 313, 380; +NAOMe: 330; +NaOAc: 330 IR (KBr) cm^{-1}: 3400 (OH), 1630 (C=O). ^1H NMR (60 MHz, CD_3OD, TMS int., δ ppm): 1.35 (3 H, *d*, $J_{6'',5''} = 6$ Hz, rhamnosyl Me), 3.3–3.6 (4 H, *m*, rhamnosyl), 3.7 (1 H, *d*, $J_{1'',2''} = 1.5$ Hz, rhamnosyl H-1''), 4.65 (1 H, *d*, $J_{2,3} = 11$ Hz, H-3), *ca* 5.1 (1 H, *d*, H-2), 6.05 (2 H, *s*, H-6, H-8), 6.65 (2 H, *s*, H-2', H-6').

Acid hydrolysis. 20 mg **2** was dissolved in 1 ml MeOH and refluxed with 3 ml 6 % HCl for 45 min. The aglycone was extracted with CH_2Cl_2 (4 × 3 ml). The aglycone was in all respects identical with dihydromyricetin (**1**) (see below). The sugar was identified as rhamnose from the H_2O phase by PC.

Methylation. 50 mg of **2** was treated with excess ethereal diazomethane soln giving a pentamethyl ether, mp 178–180°. UV λ_{max}^{MeOH} nm: 285, 320 and no bathochromic shifts with $AlCl_3$ and $AlCl_3/HCl$. MS m/z (rel. int. %): 390 (3), 372 (18), 209 (14), 181 (100).

Hydrolysis of the pentamethyl ether of **2**. 20 mg of the pentamethyl ether was hydrolysed and processed as above. UV λ_{max}^{MeOH} nm: 288, 325; $+AlCl_3$ 318, 368; $+AlCl_3/HCl$ 288, 325.

Dihydromyricetin (**1**). The 40 % methanol eluates (B) were repeatedly recrystallized from 30 % EtOH giving 0.72 g of pure **1** as pale yellow needles, mp 235–237°, decomp. (lit. 245–246° 225–227°). UV λ_{max}^{MeOH} nm: 292, 333; $+AlCl_3$ 313, 390; $+AlCl_3/HCl$ 313, 390; +NaOMe 328, 415. ^1H NMR (60 MHz, CD_3OD, TMS int., δ ppm) 4.35 (1 H, *d*, $J_{2,3} = 12$ Hz, H-3), *ca* 5 (1 H, *d*, H-2), 6.05 (2 H, *s*, H-6, H-8), 6.65 (2 H, *s*, H-2', H-6'). MS m/z (rel. int. %) 320 (27), 168 (22), 153 (53), 152 (30), 139 (100).

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ACACETIN 7-*O*-β-D-GALACTOPYRANOSIDE FROM *CHRYSANTHEMUM INDICUM*

A. CHATTERJEE, S. SARKAR and S. K. SAHA

Department of Pure Chemistry, University College of Science, 92, A.P.C. Road, Calcutta 700009, India

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Key Word Index—*Chrysanthemum indicum*; Compositae; acacetin 7-*O*-β-D-galactopyranoside.

Abstract—From the yellow flowers of *Chrysanthemum indicum*, a new flavone glycoside, acacetin 7-*O*-β-D-galactopyranoside was isolated and its structure established from spectral evidence and synthesis.

The chemical investigation of the yellow flowers of *Chrysanthemum indicum* L. (= *Dendranthema indicum* (L.) Desmoulins), which are known to be stomachic and aperient [1], led to the isolation of a new flavone glycoside, acacetin 7-*O*-β-D-galactopyranoside (**1**). In this communication we report on the chemistry and synthesis of this compound.

The colour reactions and spectral properties indicated that **1** is a flavone glycoside. **1**, $C_{22}H_{22}O_{10}$ (M^+ 446), showed UV absorption maxima characteristic of a 5-hydroxyflavone [2] and gave a bathochromic shift with $AlCl_3$. Several structural features could be ascertained from its 80 MHz ^1H NMR spectrum in DMSO-d_6. Thus, it exhibited an A_2B_2 system in the aromatic region at δ 7.96 ($C_{2'}$–H + $C_{6'}$–H) and 7.03 ($C_{3'}$–H + $C_{5'}$–H) (J = 8.0 Hz each) indicating the presence of a *para*-substituted B-ring. The two *meta*-coupled protons at C_6 and C_8 appeared at 6.75 and 6.85 (J = 2.0 Hz each), while the C_3–H resonated as a singlet at 6.38. The other singlet at 3.79 was attributed to the $C_{4'}$–OMe. Gal-H-1 resonated at 5.30 while other galactosyl protons appeared in the region 3.0–3.70. The exchangeable proton signal was observed at 12.78 for C_5–OH.

Acid hydrolysis gave acacetin, 5,7-dihydroxy-4′-methoxyflavone, which was identified from spectral studies. The sugar was characterized as galactose.

The structure of **1** was confirmed by synthesis. Wagner *et al.* [3] previously synthesized it by the coupling of 5,7-dihydroxy-4′-methoxyflavanone (isosakuranetin) and α-acetobromogalactose. We, however, prepared this compound using phloroacetophenone involving a different route. On treatment with anisoyl chloride in the presence of dry C_5H_5N, phloroacetophenone afforded 2,4,6-trianisoylphloroacetophenone which underwent Baker–Venkataraman transformation [4, 5] in powdered KOH and dry C_5H_5N to give the dibenzoylmethane derivative **2**. This, on dehydrocyclization [5] with fused NaOAc in glacial HOAc, gave acacetin. Galactosylation of acacetin was achieved by treatment with pentaacetyl-β-D-galactopyranose in the presence of BF_3/Et_2O at room temperature [7]. The 5-hydroxy-4′-methoxyflavone 7-*O*-β-D-galactopyranoside tetraacetate (**3**) thus produced was deacetylated with methanolic $KHCO_3$ solution to afford **1**. The synthetic compound was identical with the naturally occurring glycoside (co-TLC, mmp, superimposable IR spectra).

EXPERIMENTAL

The plant material was collected from the Indian Botanic Garden, Howrah, W.B., India and verified by Professor P. C. Dutta, Department of Botany, Ballygunge Science College, Calcutta. A voucher specimen has been deposited at the Department of Pure Chemistry, Calcutta University. The mps are uncorr. The UV spectra were measured in MeOH and the NMR spectra were recorded using TMS as internal standard. Column chromatography was carried out with Si gel (Gouri Chemical Works, 60–100 mesh) and TLC with Si gel G (Merck). Appropriate drying agents were used to dry organic solvents and samples were routinely dried over P_2O_5 for 24 hr.